

(19) World Intellectual Property **Organization**

International Bureau





(43) International Publication Date 25 November 2004 (25.11.2004)

PCT

(10) International Publication Number WO 2004/100885 A3

(51) International Patent Classification⁷:

A61K 31/34

(21) International Application Number:

PCT/US2004/014263

(22) International Filing Date:

7 May 2004 (07.05.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/469,233

9 May 2003 (09.05.2003)

US

- (71) Applicant (for all designated States except US): THE TRUSTEES OF THE UNIVERSITY OF PENN-SYLVANIA [US/US]; 3160 Chestnut Street, Suite 200, Philadelphia, PA 19104-6283 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): THOMPSON, Craig, B. [US/US]; 304 Mallwyd Road, Merion Station, PA 19066 (US). BAUER, Daniel [US/US]; 251 South 22nd Street, Philadelphia, PA 19103 (US). HATZI-VASSILIOU, Georgia [GR/US]; 2425 Lombard Street, Philadelphia, PA 19146 (US).
- (74) Agent: DELUCA, Mark; Cozen O'Connor, 1900 Market Street, Philadelphia, PA 19103 (US).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- (88) Date of publication of the international search report: 28 July 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR TREATING CANCER

(57) Abstract: Methods of treating individuals identified as having cancer using ATP citrate lyase inhibitor and/or tricarboxylate transporter inhibitor are disclosed. Methods of inducing apoptosis in cancer cells using an ATP citrate lyase inhibitor and/or tricarboxylate transporter inhibitor are disclosed. Methods of treating an individual who has cancer comprising the steps of identifying the cancer as having a high rate of aerobic glycolysis, and administering an ATP citrate lyase inhibitor and/or tricarboxylate transporter inhibitor are disclosed. Methods of treating individuals who have cancer using compounds that inhibit the expression of ATP citrate lyase or tricarboxylate transporter are disclosed. Methods of identifying a compound with anticancer activity are disclosed.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/14263

A. CLA	ASSIFICATION OF SUBJECT MATTER		
	: A61K 31/34		
US CL	: 514/473		
_ 	to International Patent Classification (IPC) or to both	national classification and IDC	
	LDS SEARCHED	The state of the s	
Minimum d	locumentation searched (classification system followe	d by clossification and the	
U.S. :	514/473	u by classification symbols)	
Dogumente		<u> </u>	
Documentat	tion searched other than minimum documentation to t	he extent that such documents are inclu	ded in the fields searched
Electronic d	lata base consulted during the international search (na	me of data base and, where practicable	search terms used)
Please See (Continuation Sheet	The same case and, where practicable	, scarcii terms uscu)
C. DOC	CUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where	annronriate of the relevant passages	Deleverate del N
A	Database CAPLUS on STN (Columbus, OH, USA) DN 128:290070 Van Viiman D of all	Relevant to claim No.
	Arzheimittei-Porschung, 1998, 48 (4) 396-402, ab	stract.	
A	Database EMBASE on STN (Columbus, OH, USA) Hildebrandt L. et al. Am. I. Physiol	- 1-57
A	Cen Physiol., 1995, 269/1, 38-1 (C22-C27) abstra	ct.	1
Α	Database CANCERLIT on STN (Columbus, OH,	USA) Gribble A D et al, J. Medicinal	54-57
	Chem. 1996 Aug 30, 39 (18) 3569-84, abstract.		
+			
Further	documents are listed in the continuation of Box C.	See patent family annex.	
	documents are listed in the continuation of Box C. pecial categories of cited documents:	"T" later document published after the	international filing date or priority
Sp. document	pecial categories of cited documents: defining the general state of the art which is not considered to be	"T" later document published after the date and not in conflict with the a	international filing date or priority pplication but cited to understand the
Sp. document		"T" later document published after the date and not in conflict with the apprinciple or theory underlying the	pplication but cited to understand the invention
Sp. document of particul	defining the general state of the art which is not considered to be lar relevance	"T" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance:	pplication but cited to understand the invention the claimed invention cannot be
Sp. document of particul earlier app	defining the general state of the art which is not considered to be lar relevance	"T" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance; considered novel or cannot be con	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step
Sp. A" document of particul a earlier app a document	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to	"T" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step
Sp. A" document of particul E" earlier app document	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as	"T" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance;	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be
document of particul earlier app document establish the specified)	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as	"T" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination
document of particul cr earlier app document establish the specified) document	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means	"T" later document published after the date and not in conflict with the apprinciple or theory underlying the document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled in	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination
document of particul continue earlier app document establish the specified) document establish the specified)	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the	"T" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art
document of particular earlier appropriate document establish the specified) document document document priority day	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the ne claimed	"X" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled i document member of the same pat	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art
document of particular earlier application document establish the specified) document document priority data	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the me claimed	"X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled in document member of the same path. "&" document member of the same path.	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art ent family
document of particular earlier appropriate document priority data	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the ne claimed tual completion of the international search 2004 (02.12.2004)	"X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled in document member of the same path. "&" document member of the same path.	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art ent family
document of particular earlier appropriate document establish the specified) document document priority data atte of the actument in the specified document in the specified document in the specified data attended to the actument in the specified data and main and main and main are and main attended to the specified data and main and main are and main are specified.	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the tree claimed trual completion of the international search 2004 (02.12.2004) iling address of the ISA/US	"X" later document published after the date and not in conflict with the apprinciple or theory underlying the "X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled i document member of the same pat	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art ent family
document of particular earlier appropriate document priority date of the actument me and mail	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the nee claimed tual completion of the international search 2004 (02.12.2004) iling address of the ISA/US Stop PCT, Attn: ISA/US	"X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled in document member of the same path. Date of mailing of the international set along. Authorized officer	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art ent family
document of particular earlier appropriate document priority data and mail Comment and mail	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the me claimed tual completion of the international search 2004 (02.12.2004) iling address of the ISA/US Stop PCT, Attn: ISA/US missioner for Patents	"X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled it document member of the same path document	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art ent family
document of particular earlier appropriate document priority data and mail Comment P.O. Alexa	defining the general state of the art which is not considered to be lar relevance plication or patent published on or after the international filing date which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as referring to an oral disclosure, use, exhibition or other means published prior to the international filing date but later than the nee claimed tual completion of the international search 2004 (02.12.2004) iling address of the ISA/US Stop PCT, Attn: ISA/US	"X" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered novel or cannot be conwhen the document is taken alone "Y" document of particular relevance; considered to involve an inventive combined with one or more other being obvious to a person skilled in document member of the same path. Date of mailing of the international set along. Authorized officer	pplication but cited to understand the invention the claimed invention cannot be sidered to involve an inventive step the claimed invention cannot be step when the document is such documents, such combination in the art ent family

	International application No.	
INTERNATIONAL SEARCH REPORT	PCT/US04/14263	
	•	
	•	
	•	
Continuation of B. FIELDS SEARCHED Item 3:		
REGISTRY, CAPLUS, USPATFULL PROLISHING BLOSIS CANCERLIE ACTO	TINE EMDACE SUPPLY	
ATP citrate lyase inhibitor and neoplasms, drug therapy, antagonists, inhib?, disrupt's evaluat?	block? antag?, apopto? cell death, screen?	
evaluat?		
•		
•		
Form PCT/ISA/210 (extra sheet) (January 2004)		